ORIGINAL ARTICLE

Comparison of Characteristics and Neonatal Outcomes between Late Preterm Infants and Term Infants: A Retrospective Cohort Study with Subgroup Analysis by Gestational Age

Prapaiporn Chongkongkiat, MD[1]

[1] Department of Pediatrics, King Taksin Memorial Hospital, Bangkok, Thailand

Objective: To compare neonatal outcomes between late preterm infants (LPIs) and full-term infants and to evaluate outcomes according to gestational age in the LPIs group.

Materials and Methods: The present study was a retrospective cohort study analyzed medical records of live-born infants delivered at a tertiary hospital in Thailand. Infants were classified as full-term if they were born in the $37^{0/7}$ to $41^{6/7}$ weeks or late preterm if they were born in the $34^{0/7}$ to $36^{6/7}$ weeks. Demographic data, short-term morbidities, neonatal management, and maternal characteristics were compared using chi-square tests and logistic regression. Subgroup analyses were conducted by gestational age within the LPIs group.

Results: Among 1,202 infants, including 601 full-term and 601 late preterm, LPIs had significantly higher rates of NICU admission at 12.1% versus 0.7% (OR 21.48, 95% CI 7.66 to 60.23), initial resuscitation at 11.5% versus 2.5% (OR 5.17, 95% CI 2.87 to 9.31) and prolong length of stays in days at a median of 5 (IQR 3 to 7) versus 4 (IQR 3 to 5) (p<0.001). In the LPIs group, two neonatal deaths occurred within 28 days, while no deaths were reported in the full-term infant group (p=0.499). Neonatal outcomes were significantly worse in LPIs compared to full-term infants, including respiratory distress at 32.8% versus 14.1% (OR 3.02, 95% CI 2.22 to 4.10), birth asphyxia at 3.8% versus 1% (OR 4.04, 95% CI 1.61 to 10.17), neonatal sepsis at 14.6% versus 0.5% (OR 35.41, 95% CI 10.96 to 114.35), hypoglycemia at 35.1% versus 9.8% (OR 5.04, 95% CI 3.56 to 7.14), and feeding intolerance at 7.2% versus 0.3% (OR 23.81, 95% CI 5.67 to 99.94), all p value of less than 0.05. Morbidity risk increased with decreasing gestational age within the LPIs group. Maternal diseases significantly associated with late-preterm birth included maternal preeclampsia (OR 9.64, 95% CI 4.10 to 22.66) and maternal hypertension (OR 2.74, 95% CI 1.21 to 6.20).

Conclusion: LPIs face significantly increased risks of early morbidities compared to full-term infants, particularly at lower gestational ages. Maternal complications are strongly linked to late-preterm delivery. These findings underscore the importance of targeted obstetric and neonatal strategies in mitigating the risks associated with late preterm birth.

Keywords: Late preterm infants; Full-term infants; Neonatal outcome; Neonatal morbidity; Maternal factors

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A full-term newborn is defined as an infant born at $37^{0/7}$ through $41^{6/7}$ weeks' gestation[1]. Therefore, late preterm infants (LPIs), defined as those born between $34^{0/7}$ to $36^{6/7}$ weeks' gestation, are less physiologically and metabolically mature than full-term infants. Maternal-fetal medicine (MFM) plays a crucial role in determining the best timing of deliveries, particularly when maternal or fetal complications necessitate early intervention. Furthermore, currently, advancements in reproductive technology have enabled many individuals with fertility issues to achieve pregnancy, resulting in multifetal pregnancies and preterm deliveries. Thus, the rate of preterm births has seen a continuous rise, with late preterm births accounting for approximately 70% of all preterm births across various gestational ages (GAs)[2].

In 2020, it was estimated that around 13.4 million babies were born worldwide, of which 9.9% were preterm infants. They are at high risk of both short-term and long-term complications. Common complications include respiratory issues, difficulty regulating body temperature, metabolic disturbances,

Correspondence to:

Chongkongkiat P.

Department of Pediatrics, King Taksin Memorial Hospital, Bangkok 10160, Thailand.

Phone & Fax: +66-2-4370123

Email: Chongkongkiat@hotmail.com

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and neurodevelopmental effects, such as learning disabilities and behavioral problems[3]. Previous studies about short-term and long-term complications in preterm infants often focus on newborns with a birth weight below 1,500 grams, classified as very low birth weight (VLBW), and those with a birth weight below 1,000 grams, classified as extremely low birth weight (ELBW). However, LPIs, the majority of the preterm population, also have similar complications and require significant healthcare resources for their care[2,4-9].

LPIs often have multiple health complications that affect various systems. These infants are more vulnerable to metabolic irregularities, respiratory problems, and infections, which may impact their long-term health and development[4,5]. Moreover, LPIs have a higher risk of mortality within the first 28 days of life[2,4]. LPIs often experience metabolic issues such as hypoglycemia, hypothermia, neonatal jaundice, and feeding problems[4,6-9]. The vulnerable infants have an elevated risk of early neonatal sepsis[10]. They are also susceptible to infections in various systems, such as pneumonia, meningitis, and necrotizing enterocolitis (NEC)[4,10].

Additionally, respiratory complications are common, including respiratory distress syndrome (RDS), transient tachypnea of the newborn (TTNB), persistent pulmonary hypertension of the newborn (PPHN), apnea, and pneumothorax. Many of these infants require respiratory support devices, such as mechanical ventilators, nasal continuous positive airway pressure (CPAP), or high-flow oxygen, to ensure proper oxygen saturation and stabilize breathing[11,12]. Intraventricular hemorrhage (IVH) is a significant neurological complication observed in preterm infants, with its incidence inversely related to GA. Although IVH is more commonly associated with VLBW or ELBW infants, it is also a concern in LPIs, as it may adversely affect long-term neurodevelopmental outcomes, potentially leading to motor and cognitive delays[13]. Furthermore, they are more susceptible to birth asphyxia, which may severely impact the infant's health[14,15]. Consequently, LPIs typically require specialized medical care and monitoring to ensure they reach stable health and developmental milestones. Moreover, the extended separation between mother and infant due to hospital stays can disrupt early bonding and attachment, especially for those needing treatment in the neonatal intensive care unit (NICU)[2,4].

They compared the GA each week from 34 weeks 0 days to 36 weeks 6 days, divided by GA by week $34^{0-6/7}$ weeks, $35^{0-6/7}$ weeks, and $36^{0-6/7}$ weeks, infants born at an earlier GA, have a higher risk of complications compared to those born at near term, whose physical development is more advanced[8,16]. The American Academy of Pediatrics (AAP) changed the definition of close to full term to "late preterm" from the previously used "near-term infant" so that medical personnel would be more aware and concerned about vulnerable infants. Therefore, the present study was conducted to determine the complications affecting LPIs and the results of treatment by comparing them with those of full-term births. This is to show the importance of problems that can occur in LPIs, which are found to be a large proportion of all premature infants. Understanding these risks and the effectiveness of treatments are crucial to improving neonatal care and outcomes in this vulnerable population.

Objective

The present study examined the characteristics of LPIs and their treatment outcomes in comparison to those of full-term infants.

Materials and Methods

Study design and population

A retrospective cohort study was conducted at a Pediatric care unit of sick newborn, preterm ward, and NICU, and post-partum unit at King Taksin Memorial Hospital in Bangkok, Thailand. The sample size was estimated based on four primary neonatal outcomes, hypoglycemia, feeding difficulty, non-invasive ventilator use, and hyperbilirubinemia requiring phototherapy. Among these, hyperbilirubinemia requiring phototherapy was reported at 4.7% in late preterm and 1.3% in full-term infants in a previous study by Teune et al.[4], which yielded the largest required sample size. Assuming a one-to-one ratio of late preterm to term infants, with 80% power and a 0.05 alpha level, the calculated sample size was 394 infants per group, totaling 788. According to hospital records, King Taksin Memorial Hospital has approximately 80 to 100 late preterm births per year. Therefore, all eligible LPIs born between January 1, 2019, and December 31, 2023, will be included. An equal number of term infants will be randomly selected based on the same month and year of birth.

The inclusion criteria were newly diagnosed LPIs, born between $34^{0/7}$ and $36^{6/7}$ weeks' gestation. Calculating the GA of the infant using the last menstruation period (LMP) counting and/or ultrasound during the maternal pregnancy and Ballard

Maturation Assessment (Ballard score)[17]. Then, full-term infants born between $37^{0/7}$ and $41^{6/7}$ weeks in the same month as the LPIs were randomly selected from the hospital records to form a control group. The methodology for the present study compares the characteristics and outcomes of treatment between LPIs and full-term infants. Infants were excluded if they were outborns, had congenital anomalies, had chromosome abnormalities, or did not have complete medical data.

Neonatal outcomes

Demographic information collected from medical record charts included maternal medical conditions, the use of antenatal steroids, infant's gender, birth weight (grams), length (centimeters), head circumference (centimeters), single versus multiple gestations, delivery method, Apgar scores, and antecedents for preterm delivery. The maternal health records were categorized as spontaneous premature labor, premature rupture of membranes (PROM), medically indicated deliveries, and maternal underlying diseases. The neonatal morbidities included metabolic disturbance such as hypoglycemia, anemia, polycythemia, hypothermia, and neonatal jaundice, feeding problems such as gastric residue, abdominal distension, emesis and blood in stool, infection status such as neonatal sepsis and NEC, and respiratory morbidity such as RDS, TTNB, PPHN, apnea, pulmonary air leak, and transient pulmonary hypertension, were recorded. The other neonatal morbidities, such as birth asphyxia, IVH, and retinopathy of prematurity (ROP), were reviewed. The respiratory management data, including the need for mechanical ventilation or intubation, nasal CPAP, nasal oxygen use, and surfactant administration, were recorded. Discharge status and length of stay (days) were reviewed.

Maternal baseline characteristics and clinical data

Baseline maternal characteristics for both LPIs and full-term infants were recorded. Maternal clinical data related to antecedents of preterm delivery were obtained from maternal health records. These data were categorized into the following groups, antenatal care (ANC), maternal diseases, obstetric complications such as preterm labor pain, preeclampsia, chorioamnionitis, and PROM, and medically indicated deliveries.

Statistical analysis

Baseline demographics of infants and mothers, along with clinical characteristics, were compared between late-preterm and full-term infants using independent samples t-test or Mann-Whitney U test for continuous variables and chi-square or Fisher's exact test for categorical variables, as appropriate. Odds ratios (ORs) were calculated to identify infant and maternal factors associated with late-preterm birth using a generalized linear mixed-effects model (GLMM), which accounted for the study's data structure in which twin infants shared the same maternal factors. Adjusted ORs were not reported due to collinearity among multiple covariates in the model. Additionally, a subgroup analysis was conducted within the late-preterm group. Baseline demographics, clinical characteristics, and infant outcomes were described and compared according to GA at birth of 34, 35, and 36 weeks, using ANOVA for continuous variables and chi-square or Fisher's exact test for categorical variables. A p-value of less than 0.05 was considered statistically significant.

Ethical approval

The present study was approved by the Bangkok Metropolitan Administration Ethics Committee for Human Research (BMAEC-S017hc/67_EXP). The present study involved a retrospective review of medical records; therefore, informed consent was not required from each participant.

Results

Characteristics of the study population

One thousand two hundred two infants were included in this retrospective cohort study, comprising 601 LPIs and 601 full-term infants. During the study period, 612 LPIs were born. Of these, 11 infants were excluded due to significant congenital anomalies and chromosome abnormalities, resulting in 601 eligible LPIs. An equal number of full-term infants were matched by month of birth for comparison. Baseline demographics showed no significant difference in gender distribution between the groups. Most participants were singleton births; however, multiple births of twins were significantly more common among LPIs compared to full-term infants at 4% versus 0.2% (p=0.002). Among full-term infants, the most common GAs were 38 and 39 weeks at 34.8% and 34.3%, respectively. In contrast, the majority of LPIs were born at 36 weeks of gestation, accounting for 60.7%. LPIs had significantly lower birth weight, length, and head circumference (p<0.001) and more extended hospital stay with a median 5 (IQR 3 to 7) versus 4 (IQR 3 to 5) days, p<0.001 (Table 1).

Table 1. Baseline demographic data and clinical characteristics between full-term infants and late-preterm infants (LPIs)

	Full-term infants (n=601)	Late-preterm infants (n=601)	p-value
Male sex; n (%)	320 (53.2)	339 (56.4)	0.297
GA (weeks); mean (range)	$39^{0/7}$ ($37^{0/7}$ to $41^{6/7}$)	$35^{6/7}$ ($34^{0/7}$ to $36^{6/7}$)	<0.001*
Singleton; n (%)	600 (99.8)	577 (96.0)	<0.001*
Multiple birth-twin; n (%)	1 (0.2)	24 (4.0)	0.002*
Fetal growth; n (%)			0.686
AGA	519 (86.4)	510 (84.9)	
LGA	4 (0.7)	3 (0.5)	
SGA			
• Symmetrical SGA	44 (7.3)	44 (7.3)	
• Asymmetrical SGA	34 (5.7)	44 (7.3)	
Birth weight (g); mean±SD	3,073±370	2,462±398	<0.001*
Length (cm); mean±SD	48.9±1.72	46.1±2.31	<0.001*
Head circumference (cm); mean±SD	33.2±1.33	31.4±1.52	<0.001*
Body temperature (°C); mean±SD	36.9±0.37	36.7±0.46	<0.001*
Length of stay (days); median (IQR)	4 (3 to 5)	5 (3 to 7)	<0.001*

GA=gestational age; AGA=appropriate for gestational age; LGA=large for gestational age; SGA=small for gestational age; SD=standard deviation; IQR=interquartile range

* Statistical significance

Maternal baseline characteristics and risk factors associated with late preterm birth

A statistically significant difference in maternal age was observed between the full-term and late preterm birth groups at 27.7±6.28 years (range 14 to 45) versus 28.9±6.85 years (range 14 to 47) (p=0.003. The majority of deliveries among LPIs were spontaneous preterm labor, accounting for 55.7% of cases. Furthermore, late preterm birth was significantly associated with several maternal factors and was more likely to result in cesarean delivery (p<0.001). Identified maternal factors included lack of ANC (p=0.002, OR 2.82, 95% CI 1.42 to 5.59), maternal preeclampsia (p<0.001, OR 9.64, 95% CI 4.10 to 22.66), maternal hypertension (p=0.007, OR 2.74, 95% CI 1.21 to 6.20), and maternal diabetes mellitus (p=0.049, OR 1.38, 95% CI 1.01 to 1.90). There were no significant differences between the groups in terms of maternal infection or drug abuse (Table 2).

Neonatal morbidities in LPIs compared to full-term infants

LPIs exhibited significantly higher rates of neonatal complications compared to full-term infants. Resuscitation at birth was more common in LPIs at 11.5% versus 2.5% (OR 5.17, 95% CI 2.87 to 9.31), as was admission to the NICU at 12.1% versus 0.7% (OR 21.48, 95% CI 7.66 to 60.23) (Figure 1). There were two cases of neonatal death among LPIs within the first 28 days of life, both of which were attributed to stage 3 NEC. No deaths were observed in full-term infants during the same period (p=0.499).

Respiratory morbidities were also significantly increased in LPIs at 32.8% versus 14.1% (p<0.001, OR 3.02, 95% CI 2.22 to 4.10), including TTNB at 30% versus 13.3% (p<0.001, OR 2.83, 95% CI 2.08 to 3.88), RDS at 2% versus 0% (p<0.001), and apnea at 1.5% versus 0% (p=0.004). There were no significant differences in the incidence of air leak syndromes, PPHN, or transient pulmonary hypertension. LPIs required respiratory support (OR 4.00, 95% CI 2.89 to 5.53) and ventilatory support (OR 12.39, 95% CI 7.07 to 21.72) significantly more often than term infants.

Birth asphyxia was significantly more frequent among LPIs compared to term infants, occurring in 3.8% of LPIs versus 1% of term infants (p=0.003, OR 4.04, 95% CI 1.61 to 10.17). The majority of birth asphyxia cases in both groups were mild. However, one infant in the LPIs group developed severe hypoxic-ischemic encephalopathy (HIE), necessitating therapeutic hypothermia. Grade I IVH was observed in three cases among LPIs. Notably, one additional IVH case of LPIs was complicated by hydrocephalus (p=0.124). ROP was another complication observed among LPIs in the present study. One case of stage 2 ROP was identified in an LPI born at 34 weeks' gestation, subsequently managed by the ophthalmology team.

Sepsis was diagnosed in 14.6% of LPIs, whereas only 0.5% of full-term infants were affected, corresponding to an OR of 35.41 (95% CI 10.96

Table 2. Maternal demographics and clinical characteristics between the two groups

	Full-term infants (n=601)	Late-preterm infants (n=601)	p-value
Age (years); mean±SD (range)	27.7±6.28 (14 to 45)	28.9±6.85 (14 to 47)	0.003*
Ethnicity; n (%)			0.074
Thai	361 (60.1)	392 (65.2)	
Foreign	240 (39.9)	209 (34.8)	
No antenatal care; n (%)	15 (2.5)	38 (6.3)	0.002*
Mode of delivery; n (%)			<0.001*
Normal labor	393 (65.4)	335 (55.7)	
Caesarean section	198 (32.9)	255 (42.4)	
Vacuum extraction	6 (1.0)	1 (0.2)	
Forceps extraction	4 (0.7)	10 (1.7)	
Maternal diseases; n (%)			
Maternal diabetes	113 (18.8)	141 (23.5)	0.049*
Maternal hypertension	10 (1.7)	27 (4.5)	0.007*
Maternal preeclampsia	7 (1.2)	54 (9.0)	<0.001*
Maternal drug abuse	15 (2.5)	26 (4.3)	0.112
Maternal infection			
• HIV	7 (1.2)	10 (1.7)	0.626
• Syphilis	13 (2.2)	23 (3.8)	0.22
• HBV carrier	13 (2.2)	18 (3.0)	0.466
• COVID-19	8 (1.3)	11 (1.8)	0.645
Maternal obstetric complication; n (%)			
Abnormal NST	24 (4.0)	43 (7.2)	0.024*
Chorioamnionitis	0 (0.0)	3 (0.5)	0.249
Maternal PROM	77 (12.8)	221 (36.8)	<0.001*
• PROM <18 hours	70 (11.6)	160 (26.6)	<0.001*
• PROM ≥18 hours	7 (1.2)	61 (10.1)	<0.001*
IUGR	2 (0.3)	11 (1.8)	0.025*
Amniotic fluid			0.259
• Normal	593 (98.7)	585 (97.3)	
• Oligohydramnios	7 (1.2)	13 (2.2)	
• Polyhydramnios	1 (0.2)	3 (0.5)	

HBV=hepatitis B virus; NST=non-stress test; PROM=premature rupture of membrane; IUGR=intrauterine growth restriction; SD=standard deviation
* Statistical significance

to 114.35). A higher proportion of LPIs underwent septic evaluations, specifically receiving blood culture, compared to full-term infants at 47.4% versus 15.8% (OR 4.80, 95% CI 3.66 to 6.30, p<0.001). Among LPIs, 0.7% had proven sepsis and 13.9% were diagnosed with presumed sepsis. In contrast, only 0.5% of full-term infants had presumed sepsis, and none had proven sepsis. Antibiotic treatment was administered to 14.6% of LPIs and 0.5% of full-term infants, yielding an OR of 40.78 (95% CI 12.56 to 132.43, p<0.001). Additionally, LPIs were more frequently exposed to empirical antibiotics, despite the absence of infection, compared to full-term infants, who were considered low risk at 14.1% versus 3.8% (OR 5.08, 95% CI 3.07 to 8.39).

Feeding intolerance was observed in 7.2% of LPIs compared to 0.3% of full-term infants (OR 23.81, 95% CI 5.67 to 99.94). NEC was observed in five cases among LPIs, whereas no cases were reported in full-term infants (p=0.062). Among the affected LPIs, three were managed with supportive treatment, while two required surgical intervention.

Metabolic complications were also more prevalent in LPIs. Hypoglycemia was observed in 35.1% of LPIs compared to 9.8% of full-term infants (OR 5.04, 95% CI 3.56 to 7.14). Hypothermia was also significantly higher in LPIs at 21.8% versus 9% (OR 2.88, 95% CI 2.02 to 4.12). Hyperbilirubinemia requiring phototherapy was significantly more common in LPIs compared

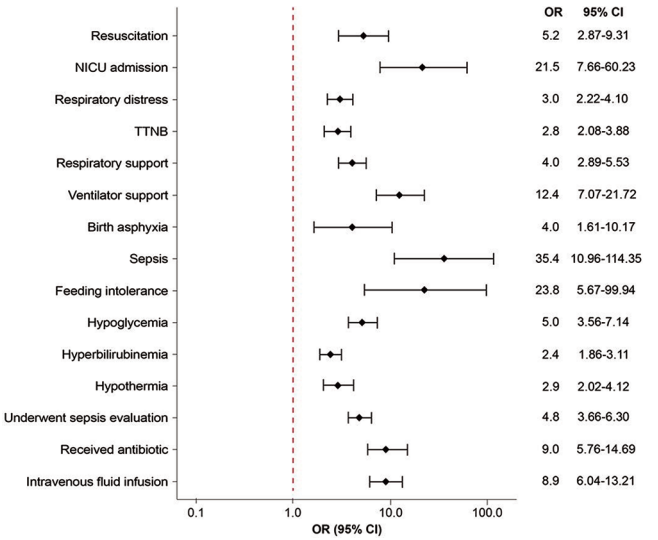

Figure 1. Odds ratios of outcomes in late preterm infants compared to full-term infants.

OR, odds ratio; CI confidence interval; NICU, neonatal intensive care unit; TTNB, transient tachypnea of the newborn

to full-term infants at 49.4% versus 29.3% (OR 2.41, 95% CI 1.86 to 3.11). The most common causes of hyperbilirubinemia in LPIs were jaundice of prematurity in 25% and breastfeeding jaundice in 16.8%. Among full-term infants, breastfeeding jaundice, at 23.5%, was the predominant cause. There were no significant differences between groups in other etiologies of jaundice, including ABO incompatibility at 1.2% versus 2.2%, glucose-6-phosphate dehydrogenase (G6PD) deficiency at 5.5% versus 3%, and extravasation of blood at 0.5% versus 0.3%. Regarding another metabolic complication, there were no significant differences between groups in the incidence of anemia or polycythemia. Additionally, LPIs required initial intravenous fluid transfusion significantly more often than full-term infants at 45.9% versus 8.8% ($p<0.001$, OR 8.93, 95% CI 6.04 to 13.21). Furthermore, 8.2% of LPIs necessitated total parenteral nutrition (TPN), whereas none of the full-term infants required this intervention ($p<0.001$) (Figure 1).

Characteristic of LPIs population according to GA at birth

Six hundred one LPIs were included in the analysis and stratified into three GA groups, $34^{0-6/7}$ weeks with 106 LPIs, $35^{0-6/7}$ weeks with 130 LPIs, and $36^{0-6/7}$ weeks with 365 LPIs. The baseline characteristics of LPIs were analyzed according to GA at birth. The proportion of singleton births increased significantly with advancing GA ($p<0.001$), while multiple births, particularly twin gestations, were most frequent at 34 weeks. Anthropometric measurements, including birth weight, length, and head circumference, showed a significant positive correlation with advancing GA ($p<0.001$). The mean birth weight increased from 2,122±350 grams at 34 weeks to 2,589±365 grams at 36 weeks. Fetal growth status differed significantly across the groups ($p=0.021$), with AGA infants constituting the majority in all groups. Although the mean body temperature did not differ significantly among groups ($p=0.335$), a wider range of temperature variation was observed in the 34-week group compared to the others (Table 3).

The length of hospital stay decreased significantly with increasing GA ($p<0.001$), with the shortest average stay observed among infants born at 36 weeks. However, nine LPIs had prolonged hospital stays exceeding 28 days, with a range of 28 to 206 days. These included three infants born at 34 weeks, one at 35 weeks, and five at 36 weeks. Notably, the most extended hospital stay, 206 days, was recorded in an infant born at 36 weeks with no ANC. This infant experienced severe birth asphyxia complicated by HIE, requiring therapeutic hypothermia. The hospital course was further complicated by respiratory distress and significant feeding intolerance, necessitating gastrostomy, fundoplication, and tracheostomy. Other causes of prolonged hospitalization included three cases with respiratory complications, two cases of late-onset hospital-acquired gram-negative septicemia, which were *Sphingomonas paucimobilis*

Table 3. Baseline demographic data and clinical characteristics of the LPIs according to gestational age at birth

Characteristic	GA $34^{0-6/7}$ weeks (n=106)	GA $35^{0-6/7}$ weeks (n=130)	GA $36^{0-6/7}$ weeks (n=365)	p-value
Male sex; n (%)	61 (57.5)	70 (53.8)	208 (57)	0.798
Singleton; n (%)	92 (86.8)	126 (96.9)	359 (98.4)	<0.001*
Multiple birth-twin; n (%)	14 (13.2)	4 (3.1)	6 (1.6)	0.001*
Fetal growth; n (%)				0.021*
AGA	88 (83.0)	111 (85.4)	311 (85.2)	
LGA	1 (0.9)	2 (1.5)	0 (0.0)	
Symmetrical SGA	7 (6.6)	4 (3.1)	33 (9.0)	
Asymmetrical SGA	10 (9.4)	13 (10.0)	21 (5.8)	
Birth weight (g); mean±SD	2,122±350	2,380±336	2,589±365	<0.001*
Length (cm); mean±SD	44.2±2.46	45.7±2.14	46.8±1.94	<0.001*
Head circumference (cm); mean±SD	30.3±1.51	31.2±1.35	31.8±1.4	<0.001*
Body temperature (°C); mean±SD	36.7±0.5	36.8±0.46	36.7±0.44	0.335
Length of stay (days); median (IQR)	8 (6 to 13)	5 (4 to 8)	4 (3 to 5)	<0.001*

GA=gestational age; AGA=appropriate for gestational age; LGA=large for gestational age; SGA=small for gestational age; SD=standard deviation; IQR=interquartile range

* Statistical significance

and *Acinetobacter baumannii*, one case of IVH with hydrocephalus, one case of persistent hypoglycemia, and one case of symmetrical small for gestational age (SGA) with VLBW at 1,360 grams.

Neonatal morbidities of LPIs according to GA at birth

Clinical outcomes varied significantly by GA. The need for resuscitation at birth was highest among infants born at 34 weeks at 30.2%, compared to 10.8% and 6.3% in the 35 and 36-week groups, respectively (p<0.001). Similarly, the rate of NICU admission declined with advancing GA, from 27.4% at 34 weeks, followed by 20% at 35 weeks and 4.9% at 36 weeks (p<0.001). Mortality within the first 28 days of life was rare and not significantly different across groups at 0.9% at 34 weeks versus 0% at 36 weeks (p=0.153) (Figure 2, Table 4).

The overall incidence of respiratory distress was highest in the 34-week group at 52.8% and significantly declined with increasing GA (p<0.001). TTNB was the most prevalent respiratory condition, affecting 50% of infants at 34 weeks compared to 23% at 36 weeks (p<0.001). Apnea was reported in 7.5% of infants at 34 weeks but not observed at 36 weeks (p<0.001). The incidences of RDS, PPHN, transient pulmonary hypertension, and air leak syndromes were low and did not differ significantly among GA groups. Regarding birth asphyxia, the overall incidence was 8.5%, 4.6%, and 2.2% in infants born at 34, 35, and 36 weeks of gestation, respectively (p=0.012). IVH occurred in 2.8% of infants born at 34 weeks, with no cases reported in

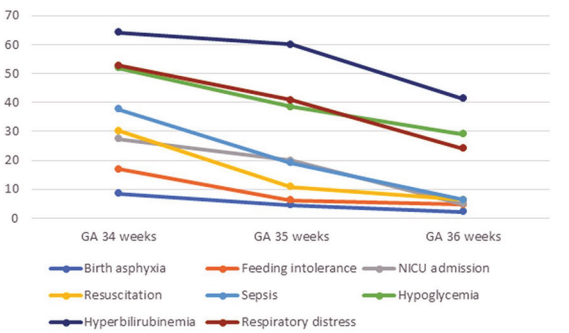

Figure 2. Late preterm outcomes by gestational age at birth. All outcomes showed a significant decreasing trend with advancing gestational age (p<0.05).

the 36-week group (p=0.007). Proven and presumed septicemia was significantly more common in infants born at 34 weeks gestation at 37.7% compared to those born at 36 weeks at 6.3% (p<0.001). The proportion of infants undergoing sepsis evaluation decreased with advancing GA 84.0% at 34 weeks, 56.9% at 35 weeks, and 33.4% at 36 weeks (p<0.001). Furthermore, NEC was most frequently observed among infants born at 34 weeks gestation, with an incidence of 2.8%, compared to 0.3% in the 36-week gestation group (p=0.028) (Table 4).

Feeding intolerance was more prevalent among infants born at 34 weeks with 17% compared to those born at 36 weeks with 4.7% (p<0.001). The incidence of hypoglycemia, a key metabolic morbidity, was highest at 34 weeks with 51.9% and declined progressively with GA, reaching 29% at 36 weeks (p<0.001). Similarly, hyperbilirubinemia requiring

Table 4. Outcomes of infants born late preterm according to gestational age at birth

Variable of outcome	GA $34^{0\text{-}6/7}$ weeks (n=106) n (%)	GA $35^{0\text{-}6/7}$ weeks (n=130) n (%)	GA $36^{0\text{-}6/7}$ weeks (n=365) n (%)	p-value
Resuscitation	32 (30.2)	14 (10.8)	23 (6.3)	<0.001*
NICU admission	29 (27.4)	26 (20.0)	18 (4.9)	<0.001*
Death in 28 days	1 (0.9)	1 (0.8)	0 (0.0)	0.153
Respiratory distress	56 (52.8)	53 (40.8)	88 (24.1)	<0.001*
RDS	3 (2.8)	6 (4.6)	3 (0.8)	1.000
TTNB	53 (50.0)	43 (33.2)	84 (23.0)	<0.001*
PPHN	0 (0.0)	1 (0.8)	1 (0.3)	0.631
Air leak	0 (0.0)	2 (1.5)	2 (0.5)	0.342
Transient pulmonary HT	0 (0.0)	4 (3.1)	3 (0.8)	0.068
Apnea	8 (7.5)	1 (0.8)	0 (0.0)	<0.001*
Respiratory support#	67 (63.2)	55 (42.3)	91 (24.9)	<0.001*
Ventilatory support	54 (50.9)	40 (30.8)	55 (15.1)	<0.001*
• Non-invasive ventilator	53 (50.0)	39 (30.0)	55 (15.1)	<0.001*
• Invasive ventilator	1 (0.9)	1 (0.8)	0 (0.0)	0.153
Birth asphyxia	9 (8.5)	6 (4.6)	8 (2.2)	0.012*
Mild	9 (8.5)	6 (4.6)	7 (1.9)	
Moderate to severe	0 (0.0)	0 (0.0)	1 (0.3)	
Infection				
Sepsis	40 (37.7)	25 (19.2)	23 (6.3)	<0.001*
NEC	3 (2.8)	1 (0.8)	1 (0.3)	0.028*
Feeding intolerance	18 (17.0)	8 (6.2)	17 (4.7)	<0.001*
Gastric residue	16 (15.1)	6 (4.6)	12 (3.3)	
Abdominal distension	6 (5.7)	3 (2.3)	4 (1.1)	
Emesis	0 (0.0)	1 (0.8)	4 (1.1)	
Blood in stool	2 (1.9)	1 (0.8)	1 (0.3)	
IVH				
IVH (any grade)	3 (2.8)	1 (0.8)	0 (0.0)	0.007*
IVH with hydrocephalus	1 (0.9)	0 (0.0)	0 (0.0)	0.176
Metabolic disturbance				
Hypoglycemia	55 (51.9)	50 (38.5)	106 (29.0)	<0.001*
Hyperbilirubinemia requires phototherapy	68 (64.2)	78 (60.0)	151 (41.4)	<0.001*
Anemia	2 (1.9)	4 (3.1)	3 (0.8)	0.117
Polycythemia	2 (1.9)	11 (8.5)	16 (4.4)	0.059
Hypothermia	28 (26.4)	24 (18.5)	79 (21.6)	0.336
Hospitalize management				
Underwent sepsis evaluation	89 (84.0)	74 (56.9)	122 (33.4)	<0.001*
Received antibiotic	66 (62.3)	47 (46.2)	60 (16.4)	<0.001*
• Treatment	40 (37.7)	25 (19.2)	23 (6.3)	
• Empirical	26 (24.5)	22 (16.9)	37 (10.1)	
Intravenous fluid infusion	86 (81.1)	69 (53.1)	121 (33.2)	<0.001*
TPN infusion	26 (24.5)	11 (8.5)	12 (3.3)	<0.001*

GA=gestational age; NICU=neonatal intensive care unit; RDS=respiratory distress syndrome; TTNB=transient tachypnea of the newborn; PPHN=persistent pulmonary hypertension of the newborn; HT=hypertension; NEC=necrotizing enterocolitis; IVH=intraventricular hemorrhage; TPN=total parenteral nutrition

"Respiratory support" includes oxygen therapy and/or ventilatory support

* Statistical significance

phototherapy was significantly more common among infants born at earlier GAs with 64.2% at 34 weeks versus 41.4% at 36 weeks; p<0.001). Among infants born at 34 weeks gestation, the predominant cause of hyperbilirubinemia was jaundice of prematurity at 53.8%. In contrast, among those born at 36 weeks, the most common cause was breastfeeding jaundice at 20.8%, followed by jaundice of prematurity at 13.2%.

Rates of anemia, polycythemia, and hypothermia did not differ significantly across the GA groups (Table 4).

LPIs at 34 weeks gestation had significantly higher rates of medical interventions compared to those at 35 and 36 weeks. Antibiotic administration was observed in 62.3% of infants at 34 weeks, compared to 46.2% at 35 weeks and 16.4% at 36 weeks ($p<0.001$). Antibiotics were given for treatment in 37.7% and empirical treatment in 24.5% of 34-week infants. Additionally, intravenous fluid infusion was required in 81.1% of infants at 34 weeks, decreasing to 53.1% at 35 weeks and 33.2% at 36 weeks ($p<0.001$). Similarly, TPN infusion was more common at 34 weeks with 24.5% compared to 8.5% and 3.3% at 35 and 36 weeks, respectively ($p<0.001$) (Table 4). These findings demonstrate that the need for intensive supportive therapies among LPIs increases as GA decreases.

Discussion

The AAP revised the terminology from "near-term infant" to "LPI" to enhance awareness among healthcare providers regarding the increased vulnerability of these infants[2]. Although LPIs are born close to term gestation, they are more likely to experience prolonged initial hospital stays and require more admission to the NICU compared to term infants[2-5]. Due to physiological immaturity, LPIs face significantly higher risks of neonatal complications that necessitate specialized care and close monitoring. In the present study, LPIs required initial neonatal care and resuscitation more frequently than full-term infants, with an OR of 5.17 (95% CI 2.87 to 9.31). Furthermore, LPIs had a markedly higher likelihood of requiring NICU admission compared to full-term infants, with an OR of 21.48 (95% CI 7.66 to 60.23). The median length of stay for LPIs is five days (IQR 3 to 7), significantly longer than for term infants, who have a mean stay of four days (IQR 3 to 5) ($p<0.001$). Among GA subgroups, infants born at 34 weeks show the highest need for initial resuscitation, NICU admission, and more extended hospital stay.

Although preterm labor pain and preterm PROM were the most common causes of late preterm delivery, with 58.9% and 36.8%, respectively, many LPIs were also born to mothers with additional risk factors compared with mother of in term pregnancies. These included maternal conditions such as diabetes mellitus, hypertension, preeclampsia, abnormal non-stress test results, and intrauterine growth restriction (IUGR). Such conditions may directly compromise fetal well-being or necessitate obstetric interventions, including early cesarean delivery. Furthermore, the absence of ANC and twin gestation were identified as additional risk factors for preterm birth, consistent with findings from previous studies[18].

Previous studies have shown that LPIs have a higher risk of neonatal death within the first 28 days of life compared to full-term infants, with a relative risk (RR) of 5.9 (95% CI 5.0 to 6.9)[4]. In the present study, two cases of neonatal death occurred among LPIs within the first 28 days of life, both due to stage 3 NEC; however, the difference compared to full-term infants was not statistically significant ($p=0.499$). Perinatal asphyxia, characterized by hypoxia or ischemia occurring during labor, in peripartum, and delivery, in intrapartum, remains a significant cause of neonatal morbidity and mortality. In neonates, oxygen deprivation can lead to multi-organ dysfunction, with the brain being particularly susceptible, resulting in HIE. Preterm infants are notably vulnerable due to their physiological and metabolic immaturity[19]. In the present study, the incidence of birth asphyxia was significantly higher among LPIs compared to term infants, occurring in 3.8% of LPIs versus 1% of term infants ($p=0.003$, OR 4.04, 95% CI 1.61 to 10.17). Notably, the LPI group had one case of severe HIE that required therapeutic hypothermia and resulted in the most extended hospitalization in this study. Previous research indicates that LPIs who experience birth asphyxia are at increased risk for neurodevelopmental challenges, including cognitive and psychomotor delays[20]. However, the present study did not assess long-term outcomes, underscoring the need for extended follow-up to evaluate the enduring impact of perinatal asphyxia in this population.

LPIs are more likely than term infants to experience neonatal morbidities during the initial birth hospitalization, including temperature instability, hypoglycemia, respiratory distress, and feeding intolerance[1,2,4,6-8]. Consistent with previous studies[2,6,7,12], LPIs in the present cohort exhibited significantly higher rates of respiratory distress (OR 3.02, 95% CI 2.22 to 4.10), particularly TTNB and RDS ($p<0.001$). These findings are likely attributable to impaired intrapulmonary fluid absorption, incomplete alveolar development, and surfactant deficiency, key factors contributing to ventilatory insufficiency in the immature lungs of preterm infants[11,21]. Apnea is also more frequent in LPIs compared to term infants. Previous studies report an incidence of 4% to 7% in LPIs versus less than 2%

at term[22]. In the present cohort, apnea of prematurity was observed in 1.5% of LPIs, whereas no cases were found among term infants (p=0.004). TTNB remains the most common cause of respiratory distress among both term and LPIs admitted to the NICU and may, in rare cases, progress to hypoxic respiratory failure due to PPHN[23]. In the present study, the rate of ventilatory support was significantly higher in LPIs compared to full-term infants (p<0.001, OR 12.39, 95% CI 7.07 to 21.72). Non-invasive ventilation was used as the first-line strategy in infants with impending respiratory failure, while only two cases of PPHN in LPIs required invasive ventilation.

Metabolic instability, particularly hypoglycemia, was a common morbidity among LPIs, consistent with previous studies linking prematurity to immature glucose homeostasis mechanisms[4-8]. A decline in glucose concentration shortly after birth may play a physiological role in triggering adaptive metabolic processes such as gluconeogenesis and glycogenolysis, which are essential for postnatal survival[24]. In the present study, the incidence of hypoglycemia among LPIs born at 34 weeks' gestation exceeded 50%, compared to 29% among those born at 36 weeks (p<0.001). Additionally, the occurrence of hypoglycemia was significantly higher in LPIs, who demonstrated a fivefold increased risk compared to full-term infants (OR 5.04, 95% CI 3.56 to 7.14).

LPIs may also be at higher risk for other metabolic disturbances, including hypothermia, hyperbilirubinemia, anemia, and polycythemia[2]. Neonatal hypothermia, defined as a body temperature below 36.5°C, is particularly concerning in LPIs. These infants possess less white adipose tissue for insulation and are less capable of generating heat through brown adipose tissue compared to full-term neonates. Furthermore, their relatively large surface area-to-body weight ratio and smaller overall size make them more susceptible to heat loss[25]. Globally, neonatal hypothermia remains a significant problem, with reported prevalence ranging from 32% to 85% in hospital settings and 11% to 92% in home births[26]. It disproportionately affects LPIs and term SGA infants. The lack of adequate thermal protection is an underrecognized but critical challenge for neonatal survival in low-resource settings. Although hypothermia is rarely listed as a direct cause of neonatal death, it significantly contributes to mortality as a comorbidity in cases of neonatal sepsis and birth asphyxia[27]. In the present study, the prevalence of hypothermia among LPIs was 21.8%, compared to 9.0% in term infants (p<0.001, OR 2.88, 95% CI 2.02 to 4.12). While global prevalence rates of hypothermia in LPIs may vary, they remain consistently higher than in full-term infants.

Similarly, the higher rate of hyperbilirubinemia observed in LPIs may reflect both increased red blood cell turnover and immature hepatic conjugation capacity. This is attributed to delayed hepatic maturation and lower concentrations of uridine diphosphoglucuronate glucuronosyltransferase (UGT), the enzyme responsible for bilirubin conjugation. LPIs are approximately twice as likely as full-term infants to exhibit significantly elevated bilirubin levels, with higher concentrations noted on days 5 and 7 after birth[28,29]. The need for phototherapy in LPIs with hyperbilirubinemia is significantly higher, at 49.4%, compared to full-term infants, at 29.3%, representing an estimated two-fold increase (p<0.001, OR 2.41, 95% CI 1.86 to 3.11). Furthermore, the requirement for phototherapy varies by GA, with rates of 64.2% at 34 weeks, 60% at 35 weeks, and 41.4% at 36 weeks of gestation (p<0.001).

Neonatal sepsis remains a leading cause of infant mortality globally, often presenting with non-specific and varied clinical signs such as temperature instability, respiratory distress, feeding difficulties, irritability, apnea, and episodes of bradycardia[10]. In the present study, the incidence of neonatal sepsis was significantly higher among LPIs compared to full-term infants at 14.6% versus 0.5% (OR 35.41, 95% CI 10.96 to 114.35). Furthermore, LPIs required more frequent septic evaluations than their full-term counterparts at 47.4% versus 15.8% (OR 4.80, 95% CI 3.66 to 6.30, p<0.001). These adverse outcomes underscore the critical need for rapid recognition of sepsis and prompt initiation of antibiotic therapy. Notably, antibiotic treatment and prophylaxis were administered more frequently in the LPIs group than in full-term infants (OR 9.02, 95% CI 5.76 to 14.69, p<0.001).

Feeding intolerance, characterized by an inability to tolerate enteral nutrition, commonly evidenced by increased gastric residuals, abdominal distension, and/or emesis is associated with increased morbidity and mortality in preterm infants. Although feeding intolerance is often a benign consequence of gastrointestinal immaturity, its clinical presentation may closely mimic the early signs of NEC, warranting vigilant assessment and differentiation[9,30]. A meta-analysis demonstrated that the prevalence of feeding intolerance among preterm infants ranged from 15% to 30%, with an overall pooled prevalence of 27%

(95% CI 23 to 31)[31]. In the present study, feeding intolerance was identified in 7.2% of LPIs and 0.3% of full-term infants, resulting in an OR of 23.81 (95% CI 5.67 to 99.94). Among LPIs, the most commonly observed symptoms were gastric residuals and abdominal distension. The prevalence of feeding intolerance was highest at 34 weeks of gestation, at 17%, followed by 6.2% at 35 weeks and 4.7% at 36 weeks.

Several conditions are primarily attributed to the relative immaturity of the pulmonary, metabolic, immune, and gastrointestinal systems in LPIs. Notably, the risk of adverse outcomes is highest among those born at 34 weeks, with a gradual improvement observed as GA increases toward 36 weeks. This gradient of risk, described in extensive epidemiological studies, underscores the heterogeneity within the LPI population[2,4,5]. Although LPIs experience better outcomes than VLBW or ELBW preterm infants, they still face a significantly higher risk of metabolic instability compared to full-term infants. This risk is often underestimated, despite evidence linking the severity of illness in LPIs to increased mortality compared to full-term counterparts[6]. This study compares neonatal outcomes between LPIs and full-term infants, highlighting higher rates of morbidity, need for resuscitation, prolonged hospital stay, NICU admission, and increased requirements for medications and ventilatory support among LPIs.

This retrospective cohort study design facilitated a comparative analysis of neonatal outcomes between LPIs and full-term infants. The study's strengths include a substantial sample size, comprehensive perinatal data, and stratified analyses based on GA. However, certain limitations should be acknowledged. Firstly, the study did not assess long-term neurodevelopmental outcomes, which are crucial given that LPIs are at increased risk for developmental disabilities, including cognitive impairments and behavioral problems. Future prospective studies should address these outcomes to provide a more comprehensive understanding of the long-term implications of late preterm birth. Secondly, the generalizability of the findings may be limited, as the research was conducted at a single tertiary-care center. Additionally, the study did not evaluate the hospital unit costs associated with treating LPIs, an important consideration given the higher healthcare expenditures linked to preterm births. Further research is warranted to assess long-term outcomes and health consequences in this population, encompassing neurodevelopmental status, growth trajectories, and academic performance.

Conclusion

The findings of the present study highlight that LPIs, particularly those born at earlier GAs, are at increased risk for short-term morbidities. Several maternal conditions, especially maternal preeclampsia and maternal hypertension, are strongly associated with late preterm birth. These results support the need for targeted antenatal risk identification, cautious decision-making regarding early delivery, and enhanced postnatal care to improve outcomes for this high-risk group. LPIs are at increased risk of neonatal morbidities compared to term infants, including temperature instability, metabolic dysregulation, respiratory distress, risk of infection, and feeding intolerance[1,2,4,6-8]. As a result, LPIs more frequently require specialized neonatal care rather than routine newborn care, as is typically sufficient for full-term infants. These morbidities often necessitate NICU admission, leading to maternal-infant separation and prolonged hospital stays. Given these challenges, both short- and long-term outcomes among LPIs warrant close evaluation. Early identification and management strategies are essential to reduce morbidity and mortality in this vulnerable population.

What is already known about this topic?

LPIs often experience multiple health complications affecting various organ systems. Compared to term infants, LPIs are at a significantly higher risk of neonatal morbidities. They are particularly vulnerable to metabolic irregularities, respiratory problems, feeding intolerance, and infections.

What does this study add?

The present study demonstrates that LPIs, particularly those born at 34 weeks, are at markedly higher risk of neonatal morbidities compared to those born at 35 and 36 weeks. Stratified subgroup analysis by GA provides new insights for targeted clinical management.

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Conflicts of interest

The author declares no conflict of interest.

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